REMARKS/ARGUMENTS

Status of the Claims

Prior to entry of this amendment Claims 107-119 were pending. Claims 113, 114, 116 and 118 are canceled. Claims 107-111, 115, 117 and 119 are amended. Support is found throughout the specification and in the claims as filed. The amendment of claim 107 adds language from previously pending claims 113. Other amendments change the claims dependency. Claim 120 is new. Support is found at least in paragraph [0088] of the application as filed. No new matter is introduced by way of this amendment. Applicants request entry of this amendment as the amendments serve to place the claims in condition for allowance or better condition for appeal.

Specification

The Examiner objected to the disclosure because it contains hyperlinks and the previous amendment did not clearly point out that the hyperlink was deleted. In response, Applicants have amended the specification by deleting reference to hyperlinks. This is evidenced in the marked-up version of the specification above. Applicants respectfully request the Examiner withdraw the objection.

New Matter/Objection to the Specification

The Examiner suggests that the previous amendment of the specification contains New Matter. The Examiner states that in response to the office action this "New Matter" must be canceled. Without agreeing with the Examiner's statements regarding the addition of the alleged "New Matter", Applicants have deleted the sequences as noted above. Applicants respectfully request the Examiner to withdraw this New Matter/Objection of the specification and the claims.

Rejections 35 U.S.C. § 112, second paragraph

Claim 119 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for the recitation "...at least about...". While Applicants respectfully disagree that this language renders the claim indefinite, Applicants have amended claim 119 to remove "about". Applicants respectfully request the Examiner to withdraw this rejection.

New Matter/Claim Rejections 35 U.S.C. § 112, first paragraph

Claims 107 and 108 and new claims 109-119 are rejected under U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Without necessarily agreeing with the propriety of the rejection, Applicants have deleted reference to SEQ ID NO:1 and SEQ ID NO:2. As such, Applicants respectfully request the Examiner to withdraw this rejection.

Rejection Under 35 U.S.C. §102

Claims 107, 109, 110 and 113-119 is rejected under 35 U.S.C. § 102(b), as being anticipated by Lowe JB[1] (U.S. Patent 5,324,663 ('663)) or Lowe[2] (U.S. Patent 5,770,420 ('420)). Applicants respectfully traverse.

Claim 107 is directed to a method for modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor, the method includes contacting a full-length recombinant glycopeptide with a reaction mixture that comprises a fucose donor moiety and a fucosyltransferase under appropriate conditions *in vitro* to transfer fucose from the fucose donor moiety to the acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern, wherein the acceptor moiety is Galβ1,4GlcNAc-OR or NeuAcα2,3Galβ1,4GlcNAc-OR, wherein R is an amino acid, a saccharide, an oligosaccharide or an aglycon group having at least one carbon atom and is linked to or is part of a glycopeptide, and wherein the eukaryotic fucosyltransferase is an isolated, recombinantly produced FucT-VI or FucT-VII fucosyltransferase, wherein the eukaryotic fucosyltransferase lacks a membrane anchoring domain, and wherein the isolated, recombinantly produced

fucosyltransferase provides at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using isolated FucT-V. This corresponds to previously pending claims 13.

While the '663 patent discloses a FucT-VI, the methods disclosed in the '663 patent are distinct from those of claim 107, and those dependent therefrom.

As the Examiner is aware, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628 (Fed. Cir. 1987).

The '663 patent fails to disclose the transfer of fucose by FucT-VI or FucT-VII to any recombinant polypeptide, wherein the isolated, recombinantly produced fucosyltransferase provides at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using isolated FucT-V. In fact, the '663 patent demonstrates a very similar level of enzyme activity between cells expressing FucT-V and FucT-VI. That is, Figure 8 depicts mean fluorescence of different cell cultures stained with antibodies against different cell surface oligosaccharide determinants (See Figure 8 and col. 3, line 57-col. 4, line 21). Only the anti-Lewis X antibody demonstrated any appreciable increase in fluorescence in the FucT-VI cultures as compared to the FucT-V cultures, yet this increase was considerably less than a two-fold increase. Otherwise, the fluorescence between the two cultures was substantially the same. However, there is *no teaching* in the '663 patent that isolated, recombinantly produced FucT-VI or FucT-VII provided 2-fold greater fucosylation of a glycopeptide as compared to fucosylation by isolated FucT-V.

In addition, the results in Table 2 demonstrate very *similar* enzyme activity between the cell extracts containing FucT-V and FucT-VI. However, there is no teaching that isolated, recombinantly produced FucT-VI or FucT-VII provided 2-fold greater fucosylation of a glycopeptide as compared to fucosylation by isolated FucT-V. Moreover, it is noted that neither Figure 8 nor Table 2 depict results when recombinant polypeptides are substrates. This is in contrast to the present claims that require transfer of fucose to a recombinant polypeptide...wherein the isolated, recombinantly produced fucosyltransferase provides at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical

conditions using isolated FucT-V. As such, the '663 patent fails to teach each element of claim 107 and those dependent therefrom.

Likewise, the '420 patent, which includes disclosure that is very similar to the '663 patent, fails to teach transfer of fucose to a recombinant polypeptide... wherein the isolated, recombinant fucosyltransferase provides at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using isolated FucT-V. As such, the '420 patent fails to teach each element of claim 107 and those dependent therefrom.

It is also noted that neither of the Lowe references disclose a FucT-VII molecule. As such, claim 110 is not anticipated by either of the Lowe references.

Moreover, even assuming, *arguendo*, that the Lowe references disclosed an *in vitro* method for fucosylation of full-length, recombinantly produced glycopeptides, a premise to which Applicants do not concede, Applicants maintain that the Lowe references fail to disclose a method in which isolated, recombinantly produced FucT-VI/FucT-VII provided at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using isolated FucT-V. At best, the Lowe references disclose cells expressing FucT-VI and FucT-V or an assay using cell extracts from cells expressing FucT-VI or FucT-V. However, it is not necessarily so that removing FucT-VI, FucT-VII or FucT-V from the cell or cell extract, e.g. isolating the enzymes, would result in a method as claimed in which isolated, recombinantly produced FucT-VI/FucT-VII provided at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using isolated FucT-V. As such, Applicants submit that the references fail to teach either explicitly or inherently the method as claimed.

Accordingly, the Lowe references fail to teach at least a method wherein isolated, recombinantly produced FucT-VI or FucT-VII provided 2-fold greater fucosylation of a glycopeptide as compared to fucosylation by isolated FucT-V under identical conditions. There is simply no teaching of such an assay; there is no disclosure of a comparison of enzymatic activities between isolated, recombinantly produced FucT-VI/FucT-VII and isolated FucT-V. Moreover, there is no demonstration in any of the Lowe references that isolated, recombinantly produced FucT-VI/FucT-VII provided at least 2-fold greater

fucosylation of the glycopeptide than is achieved under identical conditions using isolated FucT-V.

Applicants request the Examiner to withdraw the rejection.

Claim 107, 109, 110 and 113-118 are rejected under 35 U.S.C. § 102(e) as allegedly being unpatentable over Lowe (6,268,193 ('193)) or Sasaki (U.S. Patent 7,094,530 ('530)). Applicants respectfully traverse the rejection.

As noted previously and as acknowledged by the Examiner, the '193 patent appears to contain the same disclosure as the '663. As such, the response to the rejection based on the '663 patent holds true for the ''193 patent as well. This response is incorporated herein by reference. It is also noted that the Lowe reference fails to disclose a FucT-VII molecule. As such, claim 110 is not anticipated by the Lowe reference.

As above, Applicants respectfully request the Examiner to withdraw the rejection.

Claims 107, 109, 110 and 113-118 are also rejected over Sasaki ('530). Sasaki discloses a fucosyltransferase and describes the construction of cells expressing the fucosyltransferase. In addition, Sasaki discloses an analysis of expression of fucosyltransferase in a variety of cell types. However, Applicants have found no disclosure in Sasaki of an *in vitro* method to transfer fucose by isolated, recombinant FucT-VI or FucT-VII to a full-length recombinant glycopeptide. Moreover, there is no disclosure in Sasaki of a method that requires transfer of fucose by isolated, recombinant FucT-VI or FucT-VII to a recombinant polypeptide...wherein the fucosyltransferase provides at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using isolated FucT-V. Applicants submit that there is, in fact, no comparative data between the enzymatic activity FucT-V and FucT-VI in Sasaki. As such, Sasaki fails to teach each element of the claims and, therefore, fails to anticipate the present claims.

Applicants respectfully request the Examiner to withdraw this rejection. It is also noted that the Sasaki reference fails to disclose a FucT-VI molecule. As such, claim 109 is not anticipated by the Sasaki reference. Applicants request that this rejection be withdrawn.

Rejection Under 35 U.S.C. §103

Claims 107-119 are rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Lowe ('663)) or Lowe ('420) or Lowe ('193) or Sasaki ('530). Applicants respectfully traverse the rejection.

The law is clear that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones,* 21 USPQ2d 1941 (Fed. Cir. 1992). Second, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 231 USPQ 375 (Fed. Cir. 1986). Third, the prior art reference, or references when combined, must teach or suggest all the claim limitations. *In re Royk*a, 180 USPQ 580 (CCPA 1974).

In affirming the obviousness analysis that it had set forth in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), the Supreme Court has also stated that "[t]here is no necessary inconsistency between the idea underlying the TSM [i.e., teaching-suggestion-motivation] test and the *Graham* analysis." *KSR Int'l Co. v. Teleflex Inc.*, No. 04-1350, slip op. at 13 (2007). Thus, the Supreme Court has not invalidated the TSM test, but rather only rejected its "rigid" application. *See id.* at 11. An obviousness rejection continues to require an explicit analysis providing some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *See id.* at 14 (citing *In re Kahn*, 411 F.3d 977, 988 (Fed. Cir. 2006)).

The alleged *prima facie* case of obviousness here is deficient because the cited references alone, or in any combination, fail to teach each and every element found in the claims. In particular, the combination of references fails to a method that requires transfer of fucose by isolated, recombinantly produced FucT-VI or FucT-VII to a recombinant polypeptide...wherein the fucosyltransferase provides at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using isolated FucT-V. Accordingly, because each claim limitation is not disclosed in the cited references, either

alone or in combination, Applicants submit that the alleged prima facie case of obviousness is in error.

Moreover, Applicants submit that based on the teaching in the Lowe patents one of skill in the art at the time of filing the Lowe patent applications would not have been motivated to pursue the method as claimed in which the fucosyltransferase provides at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using FucT-V. That is, based on the disclosure in Lowe, as shown in Figure 8 and Table 2, in which FucT-V and FucT-VI displayed substantially similar activities, one of skill in the art would not have been motivated to continue to examine a method as claimed, which requires that FucT-VI or FucT-VII results in at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using FucT-V. Moreover, based on the teachings in Lowe, one of skill in the art would not have had a reasonable expectation of success in accomplishing a method as claimed because the teachings of Lowe demonstrate that the enzymes have substantially similar activities.

The Examiner is reminded that a prior art reference or references "must be considered in its entirety, i.e. as a whole, including portions that would lead away from the claimed invention". See MPEP 2141.02(VI), citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.* 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). Here, Applicants submit that the teaching in the Lowe patents teach away from a method wherein the fucosyltransferase provides at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using FucT-V. Again, the Lowe patents demonstrate that FucT-V and FucT-VI display similar activities when expressed in cells. As shown in Figure 8, the fluorescence was similar for all antibodies examined, with the exception of anti-LEX and for this antibody FucT-V displayed approximately 400 mean fluorescence intensity units, while FucT-VI displayed approximately 600 mean fluorescence intensity units. Clearly FucT-VI did not display 2-fold more activity than FucT-V. Moreover, the data in Table 2 demonstrate that FucT-VI had ***equal or less activity*** than FucT-V against all of the substrates in Table 2, not two-fold more activity, as set forth in the claims. Thus, based on the teachings of the Lowe patents, one of skill in the art would not have investigated a method as claimed and moreover, would not have had a

reasonable expectation of success. Applicants submit that Sasaki fails to cure this deficiency. Not until Applicants invention was it appreciated that "certain FucT molecules are surprisingly more effective at fucosylating glycopeptides." See paragraph 102. Thus, not only is the prior art lacking a teaching of each limitation of the claims, Applicants submit that there was no motivation at the time of the invention to modify the prior art to reach the presently claimed invention. In contrast, Applicants submit that the Lowe patents actually teach away from a method as claimed. As such, there is no *prima facie* case of obviousness. Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants respectfully request a telephone interview if the Examiner believes that the claims as amended are not in condition for allowance in light of the response submitted above. The undersigned can be reached at 415-442-1000.

Respectfully submitted,

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